

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants : Stanley M. Crain and Kei-Fei Shen  
 Appn. No. : Not Yet Assigned (Cont. of 09/585,517)  
 Filed : Herewith  
 For : METHOD OF SIMULTANEOUSLY ENHANCING ANALGESIC POTENCY AND ATTENUATING DEPENDENCE LIABILITY CAUSED BY MORPHINE AND OTHER BIMODALLY-ACTING OPIOID AGONISTS  
 Art Unit : 1614  
 Examiner : J. Reamer

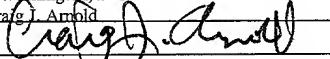
**PRELIMINARY AMENDMENT**

Commissioner of Patents  
 and Trademarks  
 Washington, D.C. 20231

Sir:

"Express Mail" mailing label no EI 647309388US  
 Date of Deposit January 3, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

Name: Craig J. Arnold  
 Signature: 

Please amend the above-identified application as follows:

**In the Specification:**

Page 1, lines 8-14, please replace the information concerning "Cross-Reference to Related Applications" with the following paragraph:

--This is a continuation of co-pending Application No. 09/585,517, filed June 1, 2000, which is a continuation of Application No. 09/094,977, filed June 16, 1998, now U.S. Patent No. 6,096,756, which is a continuation of Application No. 08/759,590, filed December 3, 1996, now U.S. Patent No. 5,767,125, which is a continuation-in-part of Application No. 08/276,966, filed July 19, 1994, which issued as

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U.S. Patent No. 5,512,578 and reissued as U.S. Reissue Patent No. 36,547, which is a continuation-in-part of Application No. 08/097,460, filed July 27, 1993, now U.S. Patent No. 5,472,943, which is a continuation-in-part of Application No. 07/947,690, filed September 19, 1992, now abandoned, the contents of which are hereby incorporated by reference in their entirety.--

In the Claims:

Please cancel Claims 1-29 without prejudice to applicants' right to pursue prosecution of these claims in a later-filed continuation application.

Please add new Claims 30-48 as follows:

30. (new) A method for selectively enhancing the analgesic potency of a bimodally-acting opioid agonist and simultaneously attenuating tolerance associated with the administration of said bimodally-acting opioid agonist, comprising administering to a subject a composition comprising an analgesic or sub-analgesic amount of said bimodally-acting opioid agonist and an amount of an excitatory opioid receptor antagonist effective to enhance the analgesic potency of said bimodally-acting opioid agonist and attenuate tolerance associated with said bimodally-acting opioid agonist.

31. (new) The method of Claim 30, wherein the excitatory opioid receptor antagonist is selected from the group consisting of naltrexone, naloxone, etorphine, diprenorphine, dihydroetorphine, and similarly acting opioid alkaloids and opioid peptides.

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32. (new) The method of Claim 30, wherein the bimodally-acting opioid agonist is selected from the group consisting of morphine, codeine, fentanyl analogs, pentazocine, buprenorphine, methadone, enkephalins, dynorphins, endorphins and similarly acting opioid alkaloids and opioid peptides.

33. (new) The method of Claim 30, wherein the amount of the excitatory opioid receptor antagonist administered is at least 100-1000 fold less than the amount of the bimodally-acting opioid agonist administered.

34. (new) The method of Claim 31, wherein the excitatory opioid receptor antagonist is naltrexone.

35. (new) The method of Claim 34, wherein the excitatory opioid receptor antagonist is naltrexone, and is administered orally.

36. (new) The method of Claim 32, wherein the bimodally-acting opioid agonist is morphine.

37. (new) The method of Claim 30, wherein the bimodally-acting opioid agonist is morphine and the excitatory opioid receptor antagonist is naltrexone.

38. (new) The method of Claim 32, wherein the bimodally-acting opioid agonist is methadone.

39. (new) The method of Claim 32, wherein the bimodally-acting opioid agonist is codeine.

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40. (new) The method of Claim 30, wherein the mode of administration is selected from the group consisting of oral, sublingual, intramuscular, subcutaneous and intravenous.

41. (new) A method for treating pain in a subject comprising administering to said subject a composition comprising an analgesic or sub-analgesic amount of a bimodally-acting opioid agonist and an amount of an excitatory opioid receptor antagonist effective to enhance the analgesic potency of said bimodally-acting opioid agonist and attenuate tolerance associated with said bimodally-acting opioid agonist.

42. (new) The method of Claim 41, wherein the bimodally-acting opioid agonist is selected from the group consisting of morphine, codeine, fentanyl analogs, pentazocine, methadone, buprenorphine, enkephalins, dynorphins, endorphins and similarly acting opioid alkaloids and opioid peptides.

43. (new) The method of Claim 41, wherein the excitatory opioid receptor antagonist is selected from the group consisting of naltrexone, naloxone, etorphine, diprenorphine and dihydroetorphine, and similarly acting opioid alkaloids and opioid peptides.

44. (new) The method of Claim 41, wherein amount of the excitatory opioid receptor antagonist administered is at least 100-1000 fold less than the amount of the bimodally-acting opioid agonist administered.

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45. (new) The method of Claim 43, wherein the excitatory opioid receptor antagonist is naltrexone.

46. (new) The method of Claim 42, wherein the bimodally-acting opioid receptor agonist is morphine.

47. (new) The method of Claim 41, wherein the bimodally-acting opioid agonist is morphine and the excitatory opioid receptor antagonist is naltrexone.

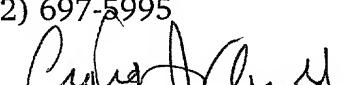
48. (new) The method of Claim 44, wherein the bimodally-acting opioid agonist is morphine and the excitatory opioid receptor antagonist is naltrexone.

REMARKS

No fee is deemed necessary in connection with this Preliminary Amendment. If any fee is required, authorization is hereby given to charge any such fee to Deposit Account No. 01-1785.

Respectfully submitted,

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New York, New York